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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
09/867,612	06/02/97	WANG	ALX-149 Y

EXAMINER: GAMBEL, P

ART UNIT	PAPER NUMBER
1644	21

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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 11/2/99; 3/25/99

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-14 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 1-14 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

–SEE OFFICE ACTION ON THE FOLLOWING PAGES–

★ U.S. GPO: 1998-404-496/40517

DETAILED ACTION

1. The Art Unit location and the examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1644.

2. The request filed 11/2/98 (Paper No. 17) for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/867,612 is acceptable and a CPA has been established An Action on the CPA follows.

Applicant's amendment, filed 3/25/99 (Paper No. 19), is acknowledged.
Claim 1 has been amended.

Claims 15 and 16 have been canceled previously.

Claims 1-14 are pending and being acted upon presently.

3. Applicant should amend the first line of the specification to update the status of the priority application, which is now abandoned.

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

5. Upon reconsideration, formal drawings, filed 9/23/94, comply with 37 CFR 1.84.

6. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Applicant is reminded that the following and should amend the specification accordingly.
The current address of the ATCC is as follows:
American Type Culture Collection, 10801 University Boulevard, Manassas, VA 20110-2209

Appropriate corrections are required

7. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-14 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed: "in a human or non-human patient ... wherein the C5 blockers does not block the functions of early complement components and does not interfere with cellular immune responses seen after immunizing mice with bovine type II collagen" .

Applicant's amendment, filed 3/25/99 (Paper No. 19), directs support to Example 3 and pages 50-51 of the specification for the written description for the above-mentioned "limitation".

However, the disclosure of "does not interfere with cellular immune responses seen after immunizing mice with bovine type II collagen" refers to the particular Examples with responses in DBA/1LacJ mice immunize with bovine collagen II.

In contrast, the instant claims appear to set forth a new subgenus by reciting "does not interfere with cellular immune responses seen after immunizing mice with bovine type II collagen in the context of "human and non-human patients" and "wherein the C5 blockers does not block the functions of early complement components" rather than the disclosure of this negative limitation in the context of the particular Examples with a particular mouse experimental model.

Applicant's reliance on generic disclosure and possibly a single species does not provide sufficient direction and guidance to the "claimed limitations" having the features currently claimed

In addition, this appears to be a negative limitation Adding the expressed exclusion of certain elements implies the permissible inclusion of all other elements not so expressly excluded. This clearly illustrates that such negative limitations do, in fact, introduce new concepts. See Ex parte Grasselli, 231 USPQ 393 (BPAI 1983).

The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Applicant is claiming a subgenus not supported by the specification as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action
Alternatively, applicant is invited to provide sufficient written support for the "limitation" indicated above.

9. Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

Applicant has not sufficient direction and guidance to enable "C5 blockers" which treat established joint inflammation "in a human or non-human patient ... wherein the C5 blockers does not block the functions of early complement components with or without the ability to interfere with cellular immune responses seen after immunizing mice with bovine type II collagen" commensurate in scope with the claimed methods. Page 25 of the specification discloses that C5 blockers comprise proteins, antibodies, peptides and other molecules (e.g. non-protein molecules) that directly interact with C5, C5a and/or C5b so as to inhibit the formation of and/or physiologic function of C5a and/or C5b. Therefore, C5 blockers cannot be considered to be limited to the specific use of C5 -specific antibodies or even K-76 COOH or substituted dihydroenzofurans as disclosed in the specification. It is not sufficient to define a specificity by its principal biological activity, e.g. C5 blockers, which in itself is ill-define, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use of the claimed C5 blockers in the claimed methods in a manner reasonably correlated with the scope of the claims broadly including any number of proteins, peptides and non-protein molecules. It has been well known in the art that minor structural differences even among structurally related compounds or compositions can result in substantially different pharmacological activities. Therefore, structurally unrelated compounds comprising antibodies, proteins, peptides and non-protein molecules would be expected to have greater differences in their activities. The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 19 24 (CCPA 1970). Without such guidance, the claimed methods employing C5 blockers would be unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Amending the claims to C5-specific antibodies would obviate this rejection.

The substitute dihydrobenzofurans and spirobenzofuran-2(3h)-cycloalkanes, as taught by Sindelar et al. (U.S Patent No. 5,173, 1499) also are considered enabled.

However, it is noted that it appears that applicant's arguments, filed 3/25/99 (Paper No. 19), appear to indicate that the inhibitors claimed and taught in methods of inhibiting inflammatory diseases including rheumatoid arthritis by Sindelar et al. (U.S. Patent No. 5,173,499) may not be predictive of the claimed methods. However, page 25 of the instant specification appears to indicate that examples of non-protein molecules that can be used as C5 blockers include K-76 COOH, substitute dihydrobenzofurans and spirobenzofuran-2(3h)-cycloalkanes, as taught by Sindelar et al. (U.S Patent No. 5,173,499). Therefore, applicant's arguments appear to be inconsistent with the specification as filed and indicate the unpredictability of the scope of any C5 blockers in the claimed methods.

Also, applicant is invited to consider to provide objective evidence to indicate and to clarify as to which specific C5 blockers disclosed in the specification as filed are also enabled in the claimed methods and amend the claims accordingly. Applicant is requested to clarify the enablements

10. Claims 1-14 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 1-14 are indefinite in that they describe the "C5 blockers" of interest by an activity only. While "C5 blockers" may have some notion of the activity of the inhibitors employed in the claimed methods; claiming biochemical molecules by a particular name or property fails to distinctly claim what that "C5 blocker" is and it is made up of. Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies the "C5 blockers" other than C5-specific antibodies, K-76 COOH, substitute dihydrobenzofurans and spirobenzofuran-2(3h)-cycloalkanes, as disclosed on page 25 of the specification.

B) Claims 1-14 are indefinite in the recitation of "in a human or non-human patient ... wherein the C5 blockers does not block the functions of early complement components and do not interfere with cellular immune responses seen after immunizing mice with bovine type II collagen" because it is not clear how the newly added limitation of "does not interfere with cellular immune responses seen after immunizing mice with bovine type II collagen" affects the metes of bounds of "C5 blockers which do not block the functions of early complement components" "in a human or non-human patient" other than "mice immunized with bovine type II collagen".

C) Claims 2-14 are indefinite in the recitation of "substantially inhibit/reduce/interfere" and "an amount sufficient ... at least 10%" because the recitation of "substantially" and "at least 10% are relative terms/phrases which renders the claimed methods indefinite. These terms/phrases are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. For example, it is not clear how the metes and bounds "substantially" differs from "an amount sufficient". Also, it is unclear what is the reference point (e.g. parameters, metes and bounds) of how "an amount sufficient" relates to "at least 10% ".

D) Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1-10 and 14 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Sindelar et al. (U.S. Patent No. 5,173, 1499). Sindelar et al. claims and teaches methods of treating patients with immune disorders or disorders involving undesirable or inappropriate complement activity, including various arthritic conditions such as rheumatoid arthritis, with dihydrobenzofurans and spirobenzofuran-2(3h)-cycloalkanes and their open chain intermediates (see entire document, including Table III, columns 2-23 and claims 3-13). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods.

For example, although Sindelar et al. does not disclose established joint inflammation per se, treating rheumatoid arthritis would have been considered as treating an established joint inflammatory disease. Although Sindelar et al. does not disclose the properties set forth in claims per se (e.g. does not interfere with cellular immune responses seen after immunizing mice with bovine type II collagen; cell-lysing ability, levels of soluble C5b-9, levels of C5, serum and synovial fluid levels, cleavage of C3) ; it appears that the dihydrobenzofurans and spirobenzofuran-2(3h)-cycloalkanes and their open chain intermediates would have had these inherent properties in methods of treating rheumatoid arthritis, absence evidence to the contrary. The burden is on the applicant to establish a patentable distinction between the claimed and referenced methods. Also, see Ex parte Novitski 26 USPQ 1389 (BPAI 1993) for the inherency of methods.

Applicant's arguments, filed 3/25/99 (Paper No. 19), as they relate to the previous rejection under 35 U.S.C. § 103(a) with respect to Sindelar et al. (U.S. Patent No. 5,173,499) have been fully considered but are not found convincing as they apply to this New Ground of Rejection under 35 U.S.C. § 102(b). It appears that applicant's arguments indicate that the inhibitors claimed and taught in methods of inhibiting inflammatory diseases including rheumatoid arthritis by Sindelar et al. (U.S. Patent No. 5,173,499) may not be predictive of the claimed methods. However, page 25 of the instant specification appears to indicate that examples of non-protein molecules that can be used as C5 blockers include dihydrobenzofurans and spirobenzofuran-2(3h)-cycloalkanes, as taught by Sindelar et al. (U.S Patent No. 5,173,499). Therefore, applicant's arguments appear to be inconsistent with the specification as filed as to whether methods of treating established joint inflammation with C5 blockers is encompassed by treating rheumatoid arthritis with non-protein molecules that can be used as C5 blockers such as dihydrobenzofurans and spirobenzofuran-2(3h)-cycloalkanes and their open chain intermediates, as taught by Sindelar et al. (U.S Patent No. 5,173,499) and relied upon in the specification as filed.

14. Claims 1-14 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Sindelar et al. (U.S. Patent No. 5,173,499; 1449) in view of Auda et al. (Rheumatol. Int.10: 185-18, 1990; 1449) , Wurzner et al. (Complement Inflamm. 8: 328-340, 1991; 1449) and Montz et al. (Cell. Immunol. 127: 337-351, 1990; 1449).

Sindelar et al. in view of Auda et al., Wurzner et al. and Montz et al. are all of record, as set forth in Paper Nos. 5/9/12/15.

Although the claims have been amended to include the recitation of "does not interfere with cellular immune responses seen after immunizing mice with bovine type II collagen"; it is not clear how this limitation would differ or would not be expected from the prior art teachings, given the recitation of treating established joint inflammation such as rheumatoid arthritis in humans, and treating inflammatory conditions such as rheumatoid arthritis as taught by the prior art of record

Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to apply C5 inhibitors including those encompassed by the dihydrobenzofurans and spirobenzofuran-2(3h)-cycloalkanes, as taught by Sindelar et al. or the anti-C5 antibodies as taught by Wurzner to treat established joint inflammation such as rheumatoid arthritis encompassed by the claimed methods and limitations with an expectation of success, given the anti-inflammatory properties of these C5 blockers essentially for the reasons of record set forth in Paper Nos. 5/9/12/15. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

15. Claims 1-14 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Sindelar et al. (U.S. Patent No. 5,173,499; 1449) in view of Auda et al. (Rheumatol. Int.10: 185-18, 1990; 1449) , Wurzner et al. (Complement Inflamm. 8: 328-340, 1991; 1449) and Montz et al. (Cell. Immunol. 127: 337-351, 1990; 1449) as applied to claims 1-14 above and in further evidence of Rollins et al. (U.S. Patent No. 5853,722)

Sindelar et al. in view of Auda et al., Wurzner et al. and Montz et al. are all of record, as set forth in Paper Nos. 5/9/12/15.

Rollins et al. has been newly added to provide further teaching and evidence that C5-specific antibodies had the property of inhibiting complement in inflammatory conditions in humans at the time the invention was made (see entire document, including Claims).

Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to apply C5 inhibitors including those encompassed by the dihydrobenzofurans and spirobenzofuran-2(3h)-cycloalkanes, as taught by Sindelar et al. or the anti-C5 antibodies as taught by Wurzner to treat established joint inflammation such as rheumatoid arthritis encompassed by the claimed methods and limitations with an expectation of success, given the anti-inflammatory properties of these C5 blockers essentially for the reasons of record set forth in Paper Nos. 5/9/12/15. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

16. Applicant's arguments, filed 3/25/99 (Paper No. 19) in conjunction with the Wang declaration under 37 C.F.R. § 1.132, filed 3/25/99 (Paper No. 18), have been fully considered but are not found convincing.

Applicant's/declarant's arguments and the examiner's rebuttal are essentially the same as of record (see Paper No. 15).

Also, it is noted that it appears that applicant's arguments appear to indicate that the inhibitors claimed and taught in methods of inhibiting inflammatory diseases including rheumatoid arthritis by Sindelar et al. (U.S. Patent No. 5,173,499) may not be predictive or read on the C5 blockers of the claimed methods. However, page 25 of the instant specification appears to indicate that examples of non-protein molecules that can be used as C5 blockers include K-76 COOH, dihydrobenzofurans and spirobenzofuran-2(3h)-cycloalkanes, as taught by Sindelar et al. (U.S Patent No. 5,173,499). Therefore, applicant's arguments appear to be inconsistent with the specification as filed and indicate the unpredictability of the scope of any C5 blockers in the claimed methods.

Also, applicant's reliance on amending the claims to include the recitation of "does not interfere with cellular immune responses seen after immunizing mice with bovine type II collagen" is acknowledged. However, it is not clear how this limitation would differ or would not be expected from the prior art teachings, given the recitation of treating established joint inflammation such as rheumatoid arthritis in humans, as it reads on the dihydrobenzofurans and spirobenzofuran-2(3h)-cycloalkanes, as taught by Sindelar et al. (U.S Patent No. 5,173) and the C5-specific antibodies as taught Wurzner et al. (Complement Inflamm. 8: 328-340, 1991) and Rollins et al. (U.S. Patent No. 5853,722)

In addition, applicant's reliance on unexpected results do not overcome clear and convincing evidence of obviousness. Also see Richardson-Vicks Inc. v. Upjohn Co., 44 USPQ2d 1181 (CAFC 1997)

Applicant's arguments are not found persuasive.

17. No claim is allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Serial No. 08/867612
Art Unit 1644

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Patent Examiner
Technology Center 1600
November 8, 1999
PHILLIP GAMBEL